

IN THE CLAIMS:

88. (Twice Amended) A purified and isolated nucleic acid sequence for bacterial expression of [encoding] a glial cell line-derived neurotrophic factor polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:6 and [further comprising] an amino-terminal methionine residue.

90. (Twice Amended) A transformed or transfected host cell [transformed or transfected with a] comprising the isolated nucleic acid of [sequence according to] Claim 88.

117. (Twice Amended) A purified and isolated DNA sequence encoding a glial cell line-derived neurotrophic factor polypeptide, wherein said nucleic acid sequence:

- (a) comprises nucleotides 304 through 705 of SEQ ID NO:3 or nucleotides 105 through 506 of SEQ ID NO:5; or
- (b) encodes a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:6; or
- (c) [encodes a polypeptide comprising an amino acid sequence which is in excess of 70% identical to an amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:6 when up to four gaps in a length of 100 amino acids may be introduced to assist in that alignment; or
- (d)] hybridizes to a nucleic acid sequence complementary to an oligonucleotide probe encoding the amino acid sequence of SEQ. ID. NO:10 [or encoding amino acids 2 to 86 of SEQ. ID. NO:4] under conditions comprising hybridizing said sequences in 6X SSPE and 0.1% SDS at 50°C [or 42°C, respectively], followed by washing in 2X SSPE and 0.1% SDS at room temperature and wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons; or
- (d) [(e)] hybridizes to a nucleic acid sequence complementary to an oligonucleotide probe encoding amino acids 2 to 86 of SEQ ID NO:4 under conditions comprising hybridizing said sequences in 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons [encodes a

polypeptide encoded by a nucleic acid sequence defined in (a), (b), (c) or (d) but differs in codon sequence due to the degeneracy of the genetic code; and wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons].

120. **(Twice Amended)** A purified and isolated nucleic acid sequence encoding a glial cell line-derived neurotrophic factor polypeptide comprising an amino acid sequence [which is in excess of 70% identical to an amino acid sequence] of SEQ ID NO:4 or SEQ ID NO:6 [when up to four gaps in a length of 100 amino acids may be introduced to assist in that alignment, and] wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

121. **(Twice Amended)** A purified and isolated nucleic acid sequence encoding a glial cell line-derived neurotrophic factor polypeptide, comprising a sequence which hybridizes to a nucleic acid sequence complementary to an oligonucleotide probe encoding the amino acid sequence of SEQ. ID. NO:10 [or encoding amino acids 2 to 86 of SEQ. ID. NO:4] under conditions comprising hybridizing said sequences in 6X SSPE and 0.1% SDS at 50°C [or 42°C, respectively], followed by washing in 2X SSPE and 0.1% SDS at room temperature, or to an oligonucleotide probe encoding amino acids 2 to 86 of SEQ ID NO:4 under conditions comprising hybridizing said sequences in 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature, and wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

122. **(Amended)** A purified and isolated nucleic acid [sequence] according to claim 117, 118, 119, 120 or 121 further comprising a codon encoding an amino-terminal methionine residue when said polypeptide is recombinantly produced by a bacterial expression system.

125. **(Twice Amended)** A purified and isolated DNA sequence encoding a glial cell line-derived neurotrophic factor polypeptide, wherein said nucleic acid sequence:

[(a)] encodes a polypeptide comprising a pre-pro form of human glial cell line-derived neurotrophic factor polypeptide as set forth in SEQ ID NO:26 amino acid residues 10 through 220 [; or

- (b) encodes a polypeptide comprising an amino acid sequence which is in excess of 70% identical to an amino acid sequence set forth in SEQ ID NO:26 amino acid residues 10 through 220 when up to four gaps in a length of 100 amino acids may be introduced to assist in that alignment; or
- (c) hybridizes to a nucleic acid sequence complementary to an oligonucleotide probe encoding the amino acid sequence of SEQ. ID. NO:10 or encoding amino acids 2 to 86 of SEQ. ID. NO:4 under conditions comprising hybridizing said sequences in 6X SSPE and 0.1% SDS at 50°C or 42°C, respectively, followed by washing in 2X SSPE and 0.1% SDS at room temperature; or
- (d) encodes a polypeptide encoded by a nucleic acid sequence defined in (a), (b) or (c) but differs in codon sequence due to the degeneracy of the genetic code; and]

wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

127. **(Amended)** A transformed or transfected host cell [transformed or transfected with] comprising a nucleic acid of [sequence according to] claim 117, 118, 119, 120 or 121.

135. **(Twice Amended)** A transformed or transfected host cell which expresses a nucleic acid sequence encoding a glial cell line-derived neurotrophic factor polypeptide, said nucleic acid sequence operatively linked to a non-native promoter, wherein said nucleic acid sequence:

- (a) comprises nucleotides 105 through 506 of SEQ ID NO:5; or
- (b) encodes a polypeptide comprising an amino acid sequence of [set forth in SEQ ID NO:4 or] SEQ ID NO:6 [; or
- (c) encodes a polypeptide comprising an amino acid sequence which is in excess of 70% identical to an amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:6 when up to four gaps in a length of 100 amino acids may be introduced to assist in that alignment; and

wherein said encoded polypeptide has the capability to promote dopamine uptake in dopaminergic neurons].

136. **(Twice Amended)** A purified and isolated nucleic acid sequence encoding a glial cell line-derived neurotrophic factor polypeptide comprising an amino acid sequence of [which is in

excess of 90% identical to an amino acid sequence of SEQ ID NO:4 or] SEQ ID NO:6 [when up to four gaps in a length of 100 amino acids may be introduced to assist in that alignment, and wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons].

138. **(Amended)** A transformed or transfected host cell [transformed or transfected with] comprising a nucleic acid of [sequence according to] claim 136.

150. **(Twice Amended)** A method for the production of glial cell line-derived neurotrophic factor polypeptide, comprising the steps of:

- (a) culturing a transformed or transfected host cell comprising a nucleic acid sequence encoding a glial cell line-derived neurotrophic factor polypeptide under conditions suitable for the expression of said polypeptide, wherein said nucleic acid sequence is operatively linked to a non-native promoter, and wherein said nucleic acid sequence is selected from the group consisting of:
  - (i) nucleotides 304 through 705 of SEQ ID NO:3 or nucleotides 105 through 506 of SEQ ID NO:5; or
  - (ii) nucleotides encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:6; [or
  - (iii) nucleotides encoding a polypeptide comprising an amino acid sequence which is in excess of 70% identical to an amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:6 when four gaps in a length of 100 amino acids may be introduced to assist in that alignment;] and
- (b) isolating said expressed polypeptide in a substantially purified form from said host cell culture [,

wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons].

151. **(Amended)** A method according to claim 150 wherein said nucleic acid [sequence] further comprises a codon encoding an amino-terminal methionine residue when said polypeptide is recombinantly produced by a bacterial expression system.

153. **(Twice Amended)** A method for the production of glial cell line-derived neurotrophic factor polypeptide, comprising the steps of:

- (a) culturing a transformed or transfected host cell comprising a nucleic acid sequence encoding a glial cell line-derived neurotrophic factor polypeptide under conditions suitable for the expression of said polypeptide, wherein said nucleic acid sequence is operatively linked to a non-native promoter, and wherein said nucleic acid sequence encodes a polypeptide having the capability to promote dopamine uptake in dopaminergic neurons and
- (i) hybridizes to a nucleic acid sequence complementary to an oligonucleotide probe encoding the amino acid sequence of SEQ. ID. NO:10 under conditions comprising hybridizing said sequences in 6X SSPE and 0.1% SDS at 50°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature; or
  - (ii) hybridizes to a nucleic acid sequence complementary to an oligonucleotide probe encoding amino acids 2 to 86 of SEQ ID NO:4 under conditions comprising hybridizing said sequences in 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature

[encodes a polypeptide comprising an amino acid sequence which is in excess of 70% identical to an amino acid sequence of SEQ ID NO:4 or SEQ ID NO:6 when up to four gaps in a length of 100 amino acids may be introduced to assist in that alignment]; and

- (b) isolating said expressed polypeptide in a substantially purified form from said host cell culture[,

wherein said polypeptide has the capability to promote dopamine uptake in dopaminergic neurons].

161. **(Amended)** A transformed or transfected host cell which expresses a nucleic acid sequence encoding a glial cell line-derived neurotrophic factor polypeptide, wherein said nucleic acid sequence encodes a polypeptide comprising an amino acid sequence of [which is in excess of 70% identical to an amino acid sequence set forth in] SEQ ID NO:4 or SEQ ID NO:6 [when up to four gaps in a length of 100 amino acids may be introduced to assist in that alignment], wherein said nucleic acid sequence is operatively linked to a non-native promoter, and wherein said encoded polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

Please cancel claims 162-164, without prejudice.